

and that its character is not far from being pathognomonic. Yet in only 3 of these 10 cases was hematuria, sufficient to be noticed by the patient, an early symptom. One other patient observed blood in the urine in considerable amounts, but some time after the onset of pain and strangury. In the 5 remaining cases whose clinical history was obtainable hematuria was late, and only slight or microscopic in quantity. It would seem that there is no clinical symptom or combination of symptoms by which we can affirm or deny the presence of a vesical carcinoma, and that the only basis for a positive diagnosis is offered us by the cystoscope and the microscope.

CONCLUSIONS. (1) Intelligent deductions and trustworthy statistics are to be derived only from careful and thorough study of a large number of cases from both the clinical and the anatomical sides. (2) The most frequent seat of carcinoma in the bladder and the direction of extension are still debatable questions. (3) Metastasis is much more frequent than is conceded by many clinicians. (4) A malignant growth in the bones may occur from a primary carcinoma of the urinary bladder. (5) The most frequent cause of death in vesical carcinoma is a secondary infection of the ascending urinary tract. (6) The diagnosis is always difficult, especially after the onset of complications.

INCOMPLETE AND COMPLETE HYPOTHYROIDŒA OR MYXŒDEMA.

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DEFICIENT secretion of the thyroid, according to the degree of subactivity and age of the subject, may cause at least three distinct clinical entities. Deficiency of secretion varying in amount from nearly normal to virtually none may produce mild nervous symptoms of a vague nature, or various grades of *myxœdema*, *idiocy*, or *cretinism*: just as an excess of secretion, or hyperthyroidœa varying in degree produces either tachycardia or profound intoxication with severe derangement of the whole body, or even death. Somewhere, then, between the normal secretion and almost total cessation of secretion, producing marked and complete myxœdema, there is a condition of subsecretion which brings about what is known in medical parlance as incomplete hypothyroidœa or "*myxœdeme fruste*." Cases of this nature are described in detail by Murray,¹ Hertoghe,² Ewald,³ Richardson,⁴ Moffitt,⁵ and Howard,⁶ and they

¹ British Med. Jour., 1898; Twentieth Century Practice of Medicine.

² Nouv. Iconographe de la Salpêtrière, 1899.

³ Die Deutsche Klinik.

⁴ The Thyroid and Parathyroid Glands, 1905.

⁵ Jour. Amer. Med. Assoc., vol. xlv, No. 12.

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have been recognized as belonging to a definite disease group, because they do not tend to progress into a condition of complete myxœdema.

This disease has many things in common with the complete form. It is more frequent in women and among those in the fourth and fifth decade, especially in those who have borne many children, or it may not occur spontaneously, and follow partial thyroidectomy. There is always some structural change in the thyroid as in complete myxœdema, and there can be no doubt as to the causal relationship between thyroid fibrosis and atrophy, and hypothyroidœa.

The symptom complex is as follows: The heart is weak and often dilated. The skin is dry and scaly, and there are curious but typical pads of fat above the clavicle. Very often there are violent joint pains, paresthesias and neuralgias. Associated with these there is a marked asthenia, subnormal temperature, great dyspnœa, and a characteristic *giving way of the knees*. There may or may not be profuse hemorrhages, either spontaneous or traumatic. In short the patient has an incomplete myxœdema without any marked myxœdematous infiltration of the skin. Given a patient with severe unaccountable dyspnœa, rheumatic pains, and sensation of being cold at all times, a physician should suspect the disease at once. It is evident that the disease is due to a subactivity, or inefficiency of the thyroid gland: (1) because there is an atrophy or fibrosis of the gland; (2) partial thyroidectomy causes it; and (3) it is relieved by the administration of thyroid extract.

In four cases described by Murray, the ages of the patients ranged from forty-four to sixty years. In Moffitt's cases, six in all, the ages at which the disease developed were from thirty-five to sixty-five years. The disease thus is one of middle life. There is sometimes a history of other thyroid disease in the family.

In general the incomplete form bears resemblance to complete myxœdema, but the symptoms are not so profound, nor are there the disfiguring spade-like hands, nor the gross, solid œdema so characteristic of the true form.

In examining a patient with hypothyroidœa the physician is often struck with the disproportion between the cardiac and the pulmonary lesions, or lack of them, and the dyspnœa which is bitterly complained of, and which is often manifest.

In most cases the heart is dilated to some degree; there is, too, a diminution in strength of the first sound. Sometimes there are faint or even marked murmurs depending upon the dilatation.

The cardiac area to the left of the sternum is generally enlarged, the impulse weak, and the pulse may be slow and feeble, or it may be rapid and weak. In the case herewith reported the pulse is never below 72 and is sometimes from 110 to 120. One of Murray's patients had a pulse of 80 to 104. Moffitt speaks of a rapid pulse in his cases. Pseudo-angina may be present and with the other neuralgias there may be anginoid pains under the left breast.

The nervous symptoms with the general asthenia are marked and distressing, the giving way of the knees is complained of very much, the patient is tired and disinclined to work. An occipital neuralgia is as often present as frontal headache. Backache, from which the patient suffers greatly, renders her nights sleepless and miserable. Indeed, the patient frequently describes the pain as being so severe that she feels as if her back was being wrenched asunder. The muscles are stiff and the joints painful early in the morning, but generally these symptoms disappear during the day. As in myxœdema the patient feels cold, and is cold, though to the examiner the skin may feel hot and dry. The mental symptoms are sometimes marked. Hallucinations of sight and hearing are common, sound of running water may apparently be heard, visions of cats, dogs, mice, and rats, or of people passing, often occur, even in bright rooms. Murray describes a case in which a marked hallucination was present; it was that of a man knocking a woman down stairs.

The facial expression is one of "sorrowful fatigue." The eyebrows are arched and the forehead wrinkled. Tinnitus aurium also annoys the patient. Murray speaks of his cases as "early thyroid fibrosis" and the thyroid is generally shrunken, hard, and difficult to palpate. The isthmus may have shrivelled up to a thin band. The skin is dry, harsh, and scaly. On removing the stockings a cloud of fine scales is often cast from them. The hair is brittle, dry, and falls out from the scalp, eyebrows, and axillæ. The hair, too, is frequently prematurely gray and white. Subconjunctival fat is yellow. Murray says that bright yellow fat is characteristic of myxœdematous cases and that thyroidectomized monkeys have vivid yellow fat. Above the clavicles are curious pads of fat which are diagnostic, and are almost always present, as in complete myxœdema. There, too, may be rolls or pads of fat above the dorsal vertebræ and over the manubrium. There also may be isolated patches of solid œdema on the abdomen.

The digestive organs are affected in several ways. In common with many asthenic diseases, hypochlorhydria is often present. In a case here described, hyperchlorhydria was a prominent symptom. The appetite is poor, there is always an obstinate constipation and frequently fecal impaction. The liver is enlarged. Transitory glycosuria sometimes occurs. The kidneys are generally sound, but the urine is scanty and high colored. Casts and albumin may appear; hematuria occurs but rarely. The respiratory apparatus is generally unaffected. The lungs may become emphysematous in elderly women. There is often during menstruation a marked huskiness of the voice which is most characteristic. Cramps or cricks of the larynx, probably neuralgic, annoy the patient, and the mucous membrane of the throat and nose becomes thickened.

Spontaneous hemorrhages may occur from any mucous membrane;

menstruation may be scanty or excessive; alarming hemorrhages sometimes occur and if the patient is pregnant, postpartum hemorrhages must be guarded against. Anemia is common in all cases of incomplete myxœdema, just as it is present in every complete form. There is always a diminution of the red cells and the hemoglobin. In both the complete and incomplete cases herein reported, changes in the morphology of the reds were striking; normoblasts, stippled cells, microcytes, and macrocytes were found. It is hard to correlate the many diverse and bewildering symptoms that occur in this protean disease, except through the fact that the *nutrition* of the nervous system, the muscles, and skin is seriously impaired. All of the symptoms depend on insufficient secretion of the thyroid gland, or of certain elements of the secretion. And it may be found that in this incomplete form one or two ingredients of the juice are lacking. The same elements that are of cardinal importance to the nutrition of the skin may not be quite so relatively deficient as those elements that have to do with the nutrition of the brain or peripheral nerves.

When we consider the numerous and highly different elements that constitute the blood plasma, the functions of which are to neutralize poisons, prevent infection, dissolve cells, and aid in the coagulation of the blood, etc., it is not hard to conceive that the growth and nutrition of the body, or that of the skin, or of the brain, depend upon just as diverse elements in the thyroid secretion as complements, hemolysins, and fibrinogens which are found in the blood plasma. If there is singleness of function of the thyroid secretion, it may be that it acts in the same way that Ehrlich's amboceptors act in serving to unite nutritious matters of the blood to cells.

Mrs. K. has the following history of invalidism for sixteen years: She is fifty-five years of age and comes of a healthy family. Her mother is still living, but her father died of sclerosis of the spinal cord. At the age of thirteen she began to menstruate, and continued to do so until she was fifty-two years of age. She has given birth to four large healthy children, and has had the usual diseases of children, pneumonia, and one very bad postpartum hemorrhage. She consulted me for her general condition, which was that of marked asthenia, with a remarkable array of symptoms apparently totally unrelated. She is not corpulent, weighing 145 pounds; is of medium height and build; is active and quick in her movements, and has no disfiguring myxœdema, in fact she is a handsome matron, and except for the anemia, is well nourished. For years she has been afflicted with an occipital neuralgia, which has been at times intractable and violent; she has also suffered from dyspnoea, joint pains, marked myalgias, giving way of the knees, and profuse uterine hemorrhages. A careful physical examination showed a weak musculature, and a harsh dry skin that scaled very easily. Her stockings

frequently contained quantities of fine, powdery scales. Above the clavicles oval pads were found, and over the abdomen there was a layer of myxoedematous infiltration. The upper eyelids were swollen and puffy. At times her feet have been oedematous. Her heart dulness was somewhat enlarged to the left, but no murmurs were found. The apex beat was weak and diffuse. The heart was evidently dilated at times.

On account of the dyspnoea, hemorrhages, and weakness of the knees, she had been compelled to remain in bed for many months out of the year. The hemorrhages lasted for three or four weeks, and were difficult to control. An examination by an expert gynecologist revealed a small polyp, the removal of which did not modify the hemorrhages. The uterus otherwise was normal. Her hair turned gray when she was thirty-five years of age, and was brittle and dry, but did not come out easily. Her pharynx and uvula were slightly swollen, and her tongue was indented. At times she has suffered from cramp of the tongue and larynx, and her voice became husky during menstruation. Her pulse was weak and rapid at times, but under thyroid extract its rate diminished. Her vessels were pliable and not atheromatous. She had had a glycosuria of short duration. Her kidneys have always been healthy, although casts were found occasionally. The specific gravity of her urine was 1030, and the amount 40 ounces in twenty-four hours.

It is said that in 20 per cent. of cases of myxoedema, casts and albumin appear in the urine. They often confuse the examiner and he is led to think that the case is nephritis. She has always had a hyperacid stomach, with some tendency to flatulency, and has been constipated, and suffered from impaction at times. Her nervous symptoms were most characteristic; she had, besides the joint pains, backache, and occipital neuralgia, hyperesthesia of the skin of the neck and supraclavicular pads, twitching eyelids, and a slight tremor of the hands, and at night would sometimes tremble for a long time without cause. An examination of her reflexes showed them to be normal. At one time it was thought she had angina pectoris, so intense was the pain in her chest under the left breast. Her joints were so painful that she could not move them, and when she arose in the morning she could hardly step on the floor on account of the pain in her soles. Her rather defective memory was the only sign of any mental involvement. She has never been mentally depressed. At times tinnitus has annoyed her. She sometimes thought she saw people in her room when it was empty. Her nights have been wretched on account of backache, tremblings in her limbs, and aching of the joints, especially of the spine. Her blood showed a moderate anemia: Hemoglobin, 76 per cent.; red cells, 3,268,000; blood index, 1.06; whites not counted. Differential count: Polymorphonuclears, 39 per cent.; lymphocytes, 59.2 per cent.; eosinophiles and myelocytes, 1.8 per cent. Nor-

moblasts, poikilocytes, macrocytes, and microcytes were seen. Numerous red cells exhibiting basophilic degeneration also were found.

Under thyroid extract many of the symptoms were relieved. She cannot tolerate much of any drug. More than 8 grains a day of the extract causes thyroidismus, which is indicated by fever and increased tremor. Under thyroid extract treatment she lost ten pounds in six weeks, but she has taken it at intervals during a year with much benefit. Her dyspnœa is less; her headaches fewer and farther apart, the tremor is gone, and her condition is generally improved. Cold East winds are trying to her still, causing joint pains and occipital neuralgia occasionally. Arsenic, iron, and strychnine have benefited her, as has general massage, which she has taken for years. The constipation was relieved by sodium glycocholate.

COMPLETE MYXŒDEMA. In contrast to the foregoing case the following one of *complete myxœdema* presents not very many differences in the subjective symptomatology, and is a typical case, especially as to the solid œdema.

Mrs. S., a large Englishwoman, aged forty-five years, mother of thirteen children, and of excellent family history, consulted me repeatedly for dyspnœa, and great weakness in the knees. I have attended her for ten years, and delivered her of her last two children. She was always healthy until the birth of her last child five years ago (when forty years of age) when she began to complain of shortness of breath and giving way of her knees. Associated with these two symptoms was a great sensitiveness to cold, even in hot summer weather. After treating her unavailingly for her dyspnœa and weakness, I discovered that she was becoming larger every month. Careful examination showed that she had become myxœmatous. Her hands were very clumsy, her legs and arms and trunk œdematous, but they did not pit on pressure. I could not palpate her thyroid. Her lungs were normal, except for a slight emphysema. Her cardiac dulness had greatly increased and a faint mitral systolic murmur appeared, her pulse was weak and flabby, her dyspnœa was so great that she could hardly walk. Her weight increased from 180 to 208 pounds. Supraclavicular swellings also developed and transitory swellings in the neck appeared over the angle of the jaw. The mucous membranes of the throat and nose became swollen. Her voice was husky, and she had scanning speech. The tongue was swollen and flabby. She complained of constant headache, and was dull and listless. She also had tinnitus aurium. Her expression was one of stupid listlessness, her forehead was wrinkled, and she looked weary and oppressed. Joint pains affected her greatly, as did a constant backache. She could not sleep and she suffered much from cold, and upon putting her hands in cold water they would swell and turn blue and were very painful. Her upper incisor teeth were stained black. This is very characteristic of myxœdema.

The urine was normal in every respect, except that it was highly colored, and of high specific gravity. She was anemic: a careful blood count on two occasions showed that she had red cells, 3,344,000; hemoglobin, 75 per cent.; white cells, 13,200 and 6900 on two occasions. A differential count showed: Polymorphonuclears, 46 per cent.; mononuclears, 52 per cent.; myelocytes and eosinophiles, 2 per cent. Stippled red cells were seen in small numbers, as were nucleated red cells. She never had any hallucinations, or severe hemorrhages; nor had she much neuralgia, suffering but twice from trifacial neuralgia.

In September, 1906, she developed a severe bronchitis, and suffered much from dyspnoea, which at that time was due to her dilated weak heart. Dr. M. Howard Fussell saw her in consultation at that time and confirmed the diagnosis of myxœdema. Thyroid extract in daily doses of 15 to 30 grains was administered for a year with very much benefit. Her dyspnoea and nervous symptoms were greatly ameliorated and she was able to move about with great comfort, but was still very myxomatous. Strophanthus and strychnine helped her a great deal. After eighteen months' treatment she became a ruddy, buxom matron again and was bright and intelligent.

The interesting features of this case are the presence of a tremor, absence of hemorrhages, the effect of the cold water on her arms, and great heart weakness.

In both cases the finding of nucleated and degenerated red cells in the blood is of interest, especially when the hemoglobin percentage was not very low. Both cases were in women who had borne numerous children, and both developed the disease when between thirty-five and forty-five years of age. Myxœdema seems to be one of the penalties of childbearing. The weak knees and heart were very prominent symptoms in both cases as was the tremor.

A METHOD OF OBTAINING CULTURES FROM HUMAN BLOOD.

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IN making cultures from the living human blood, Lenhartz and Schottmüller advised the mixing of freshly drawn blood with liquified fluid agar (at 45° C.) and the incubation of the culture at 37° C. The method has been employed by them to a large extent and numerous positive blood cultures have been obtained—in sepsis, typhoid fever, pneumonia, and other diseases associated with bacterial infection of the blood. The blood is usually drawn from a